REMARKS

Claim Objection

Claims 19-31 have been re-numbered claims 32-47, and the dependencies have been re-numbered accordingly. Former claim 22 has been divided into two claims, one including the preference of former claim 22. Each one of the former claims 28 and 30 has been divided into two claims, one including the "particularity" of such former, but in a re-arranged writing: "preparation intended for a pharmaceutical field" has been amended into "composition" and in "pharmaceutical composition". Such amendments are thought to be self-explanatory versus the former claims.

Claims rejections under 35 USC 112

It is respectfully submitted that the invention as claimed now fulfils the requirements of 35 USC 112.

Claims rejections under 35 USC 102(b) Novelty

Claims 10 to 18 were rejected under 35 U.S.C. 102(b) as being anticipated by US patent 5,573,777 to SERPELLONI et al.

The Affidavit previously filed on July 23, 2002, has been completed mainly by the preparation methods for each of the four samples and is therefore submitted as a new Affidavit.

Our arguments remain mainly as previously explained in our response to the second Office Action on July 23, 2002, as detailed below.

Reconsideration is requested for the reasons that follow:

The object of the invention is a pulverulent mannitol having the following specific combination of characteristics:

- an average diameter of between 60 and 200 μm; **and**
- a **packed bulked density**, determined according to the method specified in the operating instructions for the HOSOKAWA P.T.N powder tester, **of between 0.65 and 0.85 g/ml; and**
- a flow factor of at least 60.

Conversely, SERPELLONI et al. disclose a pulverulent mannitol having a packed bulked density lower than 0.60 g/ml, as agreed by the Examiner on page 6, line 12 of the letter mailed on March 23, 2002 and on page 5, line 15 of the letter mailed on January 10, 2003.

Thus, the pulverulent mannitol of the invention differs from the one disclosed in SERPELLONI et al. in that it has a higher packed bulked density, i.e. of between 0.65 and 0.85 g/ml.

However, the Examiner asserts that the criticality of such small difference is unclear and that any distinction is a matter of degree and not of kind.

The Applicants would like to stress that what seems to be a "*slight*" difference in the packed bulked density between the product of the invention and the product of SERPELLONI et al. leads to products which are completely different from each others.

In order to clearly demonstrate the difference between the pulverulent mannitol of the invention and the pulverulent

mannitol of SERPELLONI et al., the Applicants herewith provide an affidavit (see annex I) from Philippe LEFEVRE along with comparative tests' results (annexe II) and photographs (annexes III to VII).

Philippe LEFEVRE is a specialist in the field of pulverulent mannitol since he currently works as manager of the Pharmaceutical and Cosmetic Applications Department by ROQUETTE FRERES. For the record, ROQUETTE FRERES is world leader in many fields of sugars and hydrogenated sugars.

Philippe LEFEVRE assayed four pulverulent mannitols:

- two from SERPELLONI et al. (PEARLITOL® 100 SD - sample E 272 M - and PEARLITOL® 200 SD -sample E 455 M -) and
- two from the instant invention (Sample X 0201 and Sample X 0104).

These pulverulent mannitols correspond respectively to lots of different particle sizes: the sample X 0201 and the sample E 455 M having a particle size centered according to the same order of magnitude (respectively 178 μm and 174 μm) and the sample X 0104 and the sample E 272 M having a particle size centered according to the same order of magnitude (respectively 126 μm and 101 μm).

These pulverulent mannitols were assayed for the following characteristics:

- average diameter;
- packed density;
- flow factor; and
- rate of dissolution in water.

Please refer to the table in annex II in which the results of these assays are presented.

The packed densities of the assayed pulverulent mannitols of the invention are 0.71 and 0.72, whereas the packed densities of the pulverulent mannitols of SERPELLONI et al. are

0.54 and 0.58 g/ml, thus 0.2 g/ml lower. This difference is very significant when taking into account the fact that the pulverulent mannitol is, among others, intended to be used for filling hard capsules. A difference of 0.2 g/ml means that a hard capsule filled with the pulverulent mannitol of the invention can contain 200 mg more mannitol than the same capsule filled with the pulverulent mannitol of the prior art! Knowing that most of the hard capsules, once filled, weight less than 100 mg, this difference of packed density is extremely significant!

The difference between the pulverulent mannitol of the invention can further be visualized on the electronic microscope photos herewith provided with annexes III to VI. The annex III and IV shows particles of pulverulent mannitols of the invention (samples Sample X 0201 and Sample X 0104). The shape of said particles completely differs from the shape of the particles of the pulverulent mannitol from SERPELLONI et al. which are coarser as exhibited on annexes V and VI.

Furthermore, Annex VII shows four test-tubes each one comprising 12 grams of a different sample. The filling of the test-tube was carried out in the same way. The height of the powder within each text-tube is different from the others, showing the differences of density of the samples (see Annex I, Affidavit).

As a conclusion, the Applicants would like to emphasize once more that the "*slight*" differences in the packed bulked density reflect great differences in the structure of the particles and in the properties of the pulverulent mannitol.

The pulverulent mannitol of the invention is hence novel over the pulverulent mannitol from SERPELLONI et al.

In view of the above, it is respectfully submitted that the rejections under 35 U.S.C. 102, should be withdrawn.

REJECTIONS UNDER 35 U.S.C. 103 (a)

Claims 10-18 were rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 5,573,777 to SERPELLONI et al.

Reconsideration is requested for the reasons that follow:

The problem that the invention proposes to solve is to provide a pulverulent mannitol, which is particularly suitable for use as filling agent for small hard capsules in pharmacology.

SERPELLONI et al. relate to pulverulent mannitol with low density, i.e. packed bulked density (see column 4, line 29 and column 5, line 18). The concern of SERPELLONI et al. is to manufacture a pulverulent mannitol, which is suitable for preparing tablets and not filing capsules. SERPELLONI et al. further stress that the low density is important for suitability in the pharmaceutical field.

Conversely to this teaching, the Applicants claim a pulverulent mannitol with a relatively higher packed bulked density. Thus, even while considering the teaching of SERPELLONI et al. as helpful, the person skilled in the art would have been led in the wrong direction, i.e. lowering the packed bulked density.

Further, the Applicants have now evidenced the differences in structure and properties of the pulverulent mannitol of the invention over the pulverulent mannitol of the prior art. As already stated above, these differences result in a new product with improved properties, which allow to new applications such as the filling of hard capsules.

In view of the above, it is respectfully submitted that the rejections under 35 U.S.C. 103, should be withdrawn.

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In view of the above, it is considered that the application is now in proper form for allowance.

Favorable consideration and prompt allowance of these claims are respectfully requested.

Respectfully submitted,

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By: _____

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